

After the line beginning "Tadg15" and ending
"DWIKENTGV~ ~~~~~ ~~", please insert --(SEQ ID No: 2)--.

After the line beginning "Scce" and ending "R~~~~~
~~", please insert --(SEQ ID No: 4)--.

After the line beginning "Try" and ending "S~~~~~
~~", please insert --(SEQ ID No: 5)--.

After the line beginning "Chymb" and ending
"PWVQKILAAN ~~~~~ ~", please insert --(SEQ ID No: 6)--.

After the line beginning "Fac7" and ending "PRPGVLLRAP
FP", please insert --(SEQ ID No: 7)--.

After the line beginning "Tpa" and ending "DWIRDNMRP~
~~~~~ ~~", please insert --(SEQ ID No: 8)--.

Please amend Figure 2 as follows:

After the line ending "R D W I K E N T G V", please  
insert --(SEQ ID No: 2)--

After the line "3121  
TTCTTTTAAAAA~~AAA~~AA", insert --(SEQ ID No: 1)--

Please amend Figure 3 by inserting --(SEQ ID No: 2)--  
e "851 ENTGV".

Please amend Figure 11 as follows: In the line beginning "hTADG15 ENTGV\*" and ending "900", after "ENTGV\*", please insert --(SEQ ID No: 2)--.

In the line consisting of "mEpithin HP", after "HP" please insert --(SEQ ID No: 10)--.

Please amend Figure 12 as follows:

On the bottom of page 1, please replace FIGURE 12-1 with --Figure 12--

On page 2, after the line ending "3147", please insert --(SEQ ID No: 1)--.

On page 2, after the line ending "2900", please insert --(Seq ID No: 9)--.

On the bottom of page 2, please replace FIGURE 12-2 with --Figure 12 (continued)--

#### REMARKS

#### Objections to the Oath or Declaration

A replacement Combined Declaration and Power of Attorney is enclosed herewith. The Applicants respectfully request that the objection to the oath or declaration be withdrawn.

### Objections to the Drawings

The drawings are objected to for various informalities. Figures 1, 2, 3, 11 and 12 have been amended herein. The changes to the figures are indicated in red on the enclosed copies and have only been made to introduce sequence identifiers into Figures 1, 2, 3, 11 and 12. Formal drawings will be submitted upon acceptance of the instant application.

### Objections to the Specification

The abstract has been objected to for not making reference to the claimed invention. This objection is respectfully traversed. The abstract has been amended to include the sentence --The instant invention also includes a kit containing antibodies for the detection of TADG-15 protein.-- Since, as amended, the abstract describes the instant invention, the Applicants respectfully request that the objection to the abstract be withdrawn.

The title has been objected to as not descriptive. This objection is respectfully traversed. The title has been amended herein. Therefore, the Applicants respectfully request that the objection to the title be withdrawn.

The disclosure has been objected to because the brief description of the figures lacks separate descriptions of Figures 12-1 and 12-2. This objection is respectfully traversed.

Figure 12 is improperly labeled as Figure 12-1 and 12-2. Figures 12-1 and 12-2 simply refer to the first and second pages of the same figure. Figure 12 has been amended herein to replace “Figure 12-1” with --Figure 12-- and “Figure 12-2” with --Figure 12 (continued)--. These changes are indicated in red on the enclosed copy of Figure 12. As such, the brief description of the figures is correct as is. Therefore, the applicants respectfully request that this objection to the disclosure be withdrawn.

#### The 35 USC §112 Rejection

Claims 22-24 stand rejected under 35 USC §112, second paragraph, as indefinite. This rejection is respectfully traversed.

First of all, the Examiner states that the recitation “TADG-15” in claims 22 and 24 is vague and indefinite. Therefore, claims 22 and 24 have been amended herein to include the full name of the protein, i.e. Tumor Antigen Derived Gene-15. The Examiner also states that the recitations “fragment thereof” in claims 22 and 24 is vague and indefinite. Therefore, amendments

have been made herein to delete this recitation from claims 22 and 24. As amended, claims 22 and 24 are no longer vague and indefinite. Therefore, the Applicants respectfully request that the 35 USC §112, second paragraph, rejection of claims 22-24 as indefinite be withdrawn.

#### The 35 U.S.C. §103 Rejections

Claims 22-24 stand rejected under 35 U.S.C. §103(a), as unpatentable over GenBank Accession Number **W22987** (October 8, 1997), in view of **Lerner** (Nature 299:592-596, 1982). This rejection is respectfully traversed.

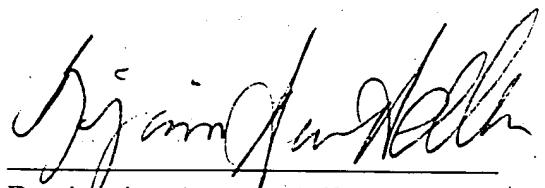
**W22987** describes the sequence of a serine protease expressed in the human colon carcinoma cell line COLO 201. This serine protease is identical to amino acids 615-855 of TADG-15. **Lerner** describes methods of generating antibodies of predetermined specificity to various antigens. The Examiner contends that it would be obvious to use the teachings of **Lerner** to generate an antibody against all or part of **W22987** to obtain an antibody against TADG-15 to incorporate into the kit of the instant invention. The Applicants respectfully disagree.

Claims 22 and 24 explicitly state that the antibody in the kit is "specific for TADG-15." An antibody raised against **W22987** would not fit this criterion. Amino acids 615-815 correspond to the serine protease domain of TADG-15. As evidenced by Figure 1 of the instant specification, this domain is highly homologous to a number of other known serine proteases. Thus, this would not be the best segment to use to obtain an antibody specific for TADG-15. TADG-15 contains a number of domains which are not present in either **W22987** or the other serine proteases of Figure 1. Therefore, given the knowledge that TADG-15 is 100% identical to another known protease starting after residue 615, it would be obvious that an antibody specific for TADG-15 must be generated from amino acid sequences before 615. Also, the Examiner seems to be implying that **W22987** is a fragment of TADG-15. However, no evidence or suggestion that this is the case can be gleaned from the combination of **W22987** and Lerner. Rather, **W22987** presents the protein as a small, complete protease. However, even if it is a fragment of a larger protease, there is no suggestion that it is a fragment of TADG-15. Therefore, the applicant respectfully requests that the 35 U.S.C. §103(a) rejection of claims 22-24 under

as unpatentable over GenBank Accession Number **W22987** in view  
of **Lerner** be withdrawn.

This is intended to be a complete response to the Office Action mailed June 29, 2000. If any issues remain outstanding, the Examiner is respectfully requested to telephone the undersigned attorney of record for immediate resolution.

Respectfully submitted,



Benjamin Aaron Adler, Ph.D., J.D.  
Registration No. 35,423  
Counsel for Applicant

Date: Sept 27, 2000  
McGREGOR & ADLER, LLP  
8011 Candle Lane  
Houston, Texas 77071  
(713) 777-2321  
[badler1@houston.rr.com](mailto:badler1@houston.rr.com)



DOCKET NO: D6064CIP

## COMBINED DECLARATION AND POWER OF ATTORNEY

Timothy J. O'Brien and Hirotoshi Tanimoto, as below-named inventors, hereby declare that: our residences, post office address and citizenship are as stated below next to our names; we believe we are the original, first and joint inventors of the subject matter which is claimed and for which a patent is sought on the invention entitled *TAP-G-15: An Extracellular Serine Protease Overexpressed in Carcinomas*, USSN 09,421,213 filed October 20, 1999.

We hereby state that we have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above. We acknowledge the duty to disclose all information we know to be material to patentability in accordance with Title 37, Code of Federal Regulations, §1.56(a), including information which became known to us between the filing date of the prior application and the national or PCT international filing date of this patent application.

We hereby appoint the following attorneys and/or agents to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith: Dr. Martin L. McGregor, Registration No. 29,239 and Dr. Benjamin Adler, Registration No. 35,423. Address all telephone calls to telephone number 713/777-2321. Address all correspondence to, McGREGOR & ADLER, 8011 Candle Lane, Houston, TX 77071.

We hereby declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

Full Name of Inventor: Timothy J. O'Brien

Inventor's Signature: Timothy J. O'Brien Date: Aug 24 2000

Residence Address: 2610 North Pierce, Little Rock, Arkansas 72207

Citizen of: United States of America

Post Office Address: 2610 North Pierce, Little Rock, Arkansas 72207

Full Name of Inventor: Hirotoshi Tanimoto

Inventor's Signature: Hirotoshi Tanimoto Date: 8/25/2000

Residence Address: 701 Green Mountain Dr., Apt. # 804, Little Rock, Arkansas 72211

Citizen of: Japan

Post Office Address: 701 Green Mountain Dr., Apt. # 804, Little Rock, Arkansas 72211

New Address: Nakabu-cho 1-5-53-401, Marugame, Kagawa 763-0033, JAPAN

*743*

Heps RIVGGGRDTSL GRWPWQVSL. .... RYDG.A HLCCGSLLSG DWVLTAACF PE.... RNRV LSRWRVFAGA VAQASPHGLQ  
 Tadg15 RVVGGTDADE GEWPWQVSL. .... HALGQG HICGASLISP KWLVSAAHCY IDDPGFRYSD PTQWTAFLGL HDQSORSAPG  
 Scce KIIDGAPCAR GSHPWQVAL. .... LSGNQL H.CGGVLVNE RWVLTAAC. .... K MNEYTVHLGS DTLG.. DR.R  
 Try KIVGGYNEE NSVPYQVSL. .... NSGYHF ..CGGSLINE QWVVSAGHC. .... Y KSRIQVRLGE HNIEVLEG.N  
 Chymb RIVNGEDAVP GSWPWQVSL. .... QDKTGF HFCGGSLISE DWVVTAAC. .... GV RTSDVVVAGE FDQGSDEE.N  
 Fac7 RIVGGKVCPL GECPWQVLL. .... LVNG.A QLCGGTLINT IWVVSAAHCF DKIKNWRNLI .... AVLGE HDLSEHDGDE  
 Tpa RIKGGLFADI ASHPWQAAIF AKHRRSPGER FLCGGILISS CWILSAAHCF QERFPFHHL. .... TVILGR .TYRVPGE

\*  
 Heps LGVOAVVYHG GYLFRDPNS EENSNDIALV HLSS.PLPLT EYIQPVCLPA ... AGQALVD GKICTVTGWG NTQYYGQQ.A  
 Tadg15 VQERRLKRII SHPFNDFTF D... YDIALL ELEK.PAEYS SMVRPICLPD ... ASHVFPKA GKAIWVTGWG HTQYGGTG.A  
 Scce AORIKASKSF RHPGYSTQT. .. HVNDMLV KLNS.QARLS SMVKKVRLPS ... RCE..PP GTTCTVSGWG TTTSPDVTFP  
 Try EQFINAAKII RHPQYDRKT. .. LNNNDIMLI KLSS.RAVIN ARVSTISLPT ... APP..AT GTKCLISGWG NTASSGADYP  
 Chymb IQVLKIAKVF KNPKFSILT. .. VNNDITLL KLAT.PARFS QTWSAVCLPS ... ADDDFPAA GTLCATTGWG KTKYNANKTP  
 Fac7 QSRRVAQVII P.... STYVP GTTNHDIAALL RLHQ.FVVLT DHVVPLCLPE RTFSERTLAF VRFSLVSGWG QLLDRGATAL  
 Tpa EQKFEVEKYI VHKEFDDDTY D... NDIALL QLKSDSSRCA QESSVVRTVC LPPADLQLPD WTECELSGYG KHEALSPFYS

\*  
 Heps GVLQEAWVPI ISNDVCNGAD FYGN..QIKP KMFCAGYPEG G..... IDA CQGDGGPV CEDSISRTPR WRLCGIVSWG  
 Tadg15 LILQKGEIRV INQTC..N LLPQ..QITP RMMCVGFLSG G..... VDS CQGDGGPL. ..SSVEADGR IFQAGVVSWG  
 Scce SDLMCVDVKL ISPQDCTKV. .YKD..LLEN SMLCAGIPDS K..... KNA CNGDGGPLV C....R.... GTLQGLVSWG  
 Try DELQCLDAPV LSQAKCEAS. .YPG..KITS NMFCVGFLLEG G..... KDS CQGDGGPVV C....N.... GQLQGVVSWG  
 Chymb DKLQQAAALPL LSNAECKKS. .WGR..RTD VMICAG..AS G..... VSS CMGDGGPLV. C.... QKDGA WTLVGIVSWG  
 Fac7 ELMVLNVPRL MTQDCLQQSR KVGDSPNITE YMFCAGYSDG S..... KDS CKGDGGP.. ..HATHYRGW WYLTGIVSWG  
 Tpa ERLKEAHVRL YPSSRCTSQH LLNRT..VTD NMLCAGDTRS GGPQANLHDA CQGDGGPLV CLN.... DGR MTLVGIVSWG

Heps T.GCALAQKP GVYTKVSDFR EWIFQAICKH SEASGXUTQL -- (SEQ ID No: 3)  
 Tadg15 D.GCAQRNKP GVYTRLPLFR DWIKENTGV~ ----- -- (SEQ ID No: 2)  
 Scce TFP CGQFNPD GVY TQVCKFT KWINDTMKKH R----- -- (SEQ ID No: 4)  
 Try D.GCAQKNKP GVYTKVNYV KWIKNTIAAN S----- -- (SEQ ID No: 5)  
 Chymb SDTCS.TSSP GVYARVTKLI PWVQKILAAN ----- -- (SEQ ID No: 6)  
 Fac7 Q.GCATVGHF GVYTRVSQYI EWLQKLMRSE PRPGVILLRAP FP (SEQ ID No: 7)  
 Tpa .LGCGQKDPV GVYTKVNTYL DWIRDNMNP~ ----- -- (SEQ ID No: 8)

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FIGURE 1



## FIGURE 2

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|     |                                                                                                                        |   |
|-----|------------------------------------------------------------------------------------------------------------------------|---|
| 1   | MGSDRARKGG GGPKDFGAGL KYNSRHEKVN GLEEGVEFLP VNNVKKKVEKH                                                                | 1 |
| 51  | GPGRIVVLA VLIIGLLVIL GIGELV <sup>N</sup> HLQ YRDVRVQKV <sup>F</sup> NGYMRITNEN                                         |   |
| 101 | FVDAYENS <sup>S</sup> NS T <sup>E</sup> FVSLASKV KDALKL <sup>L</sup> LYSG VPFLGPYHKE SAVTAFSEGS                        | 2 |
| 151 | VIAYYWSEFS IPQHVLVEEAE RVMAEERVVMM LPPRARS <sup>I</sup> K <sup>S</sup> FVVT <sup>S</sup> VVAFF                         |   |
| 201 | TDSKTVQRTQ DNS <sup>C</sup> SFGLHA RGVELMRF <sup>T</sup> PGFPDSPYPA HAR <sup>C</sup> QWALRG                            |   |
| 251 | DADSVVL <sup>S</sup> LTF RSFDLAS <sup>C</sup> DE RGSDLV <sup>T</sup> VYN TLSPMEPHAL VQL <sup>C</sup> GTYPPS            | 3 |
| 301 | <sup>Y</sup> NLT <sup>E</sup> FHSSQN VLLITLITNT ERRHPGF <sup>E</sup> AT FFQLPRMSSC <sup>*</sup> GGRLRKAQGT             |   |
| 351 | FNSPYYPGHY PPNID <sup>C</sup> TWN <sup>I</sup> EVPNNQHV <sup>K</sup> V SFKFFY <sup>L</sup> LEP GPAGT <sup>C</sup> PKD  |   |
| 401 | YVEINGEKY <sup>C</sup> GERSQFVVTS NSNKITVRFH SDQSYTDTGF LAEYLSYDSS                                                     |   |
| 451 | DPCPGQFTCR TGRCIRKELR CDGWADCTDH S <sup>E</sup> DELNCSCDA GHQFTCKNK <sup>F</sup>                                       |   |
| 501 | CKPLFWVCDS VNDCGDN <sup>S</sup> DE QGCCSCPAQT <sup>F</sup> RCSNGKCLSK SQQCNGKDDC                                       | 4 |
| 551 | GDG <sup>S</sup> DE <sup>A</sup> SCP KVNVVTCTKH TYRC <sup>L</sup> NLCL SKGNPECDGK EDCSDC <sup>S</sup> DEK              |   |
| 601 | DCDCGLRSFT RQAR <sup>Y</sup> VGGTD ADEGEWPWQV SLHALGQGH <sup>I</sup> CGASLISPNW                                        |   |
| 651 | LVSA <sup>A</sup> H <sup>E</sup> CYID DRGFRYS <sup>D</sup> P <sup>T</sup> QWTAFLGLHD QSQR <sup>S</sup> APGVQ ERLKRIISH |   |
| 701 | PFENDFTFDY @IALLELEKP AEYSSMVRPI CLPDASHVFP AGKAIWVTGW                                                                 |   |
| 751 | GHTQYGGTGA LILQKG <sup>E</sup> IRV INQTTCENLL PQQITPRMMC VGFLSGGVDS                                                    |   |
| 801 | CQG <sup>E</sup> S <sup>S</sup> GPLS SVEADGRIFQ AGVVS <sup>W</sup> GDDGC AQRNKP <sup>G</sup> VYT RLPLFRDWIK            |   |
| 851 | ENTGV <sup>V</sup> (SEQ ID No. 2)                                                                                      |   |

3

- : Conserved cysteine residue
- NXT : Possible N-linked glycosylation site
- SDE : Conserved SDE motif
- ▼ : Potential cleavage site
- O : Conserved amino acids of catalytic triad H, D, S

1. Cytoplasmic domain
2. Transmembrane domain
3. CUB repeat
4. Ligand-binding repeat (class A motif) of LDL receptor like domain
5. Serine protease

FIGURE 3

hTADG15 MGSLRARKGG GGPKDFGAGL KYNSRHEKVN GLEEGVEFLP VNNVKKVEKH 50  
 mEpithin ---N-G--A- --SQ----- --D--L-NM- -F----- A--A----R

hTADG15 GPGRWVVLAAL VLIGLLLVL GIGFLVWHLQ YRDVRVQKVF NGYMRITNEN/100  
 mEpithin --R-----V- --FSF--LS- MA-L---FH --N----- --HL----I

hTADG15 FVDAYENSNS TEFVSLASKV KDALKLLYSG VPFLGPYHKE SAVTAFSEGS 150  
 mEpithin -L-----T- ---I---Q- -E-----NE --V-----K -----

hTADG15 VIAYYWSEFS IPQHLVEEAE RVMAEERVVM LPPRARSLKS FVVTSVVAFP 200  
 mEpithin ----- --P--A--VD -A--V----T -----A--- --L-----

hTADG15 TDSKTVQRTQ DNSCSFGLHA RGVELMRFTT PGFPDSPYPA HARCQWALRG 250  
 mEpithin I-PRML----- A--- H-AAVT----- N----- V-----

hTADG15 DADSVLSLTF RSFDLASCDE RGSDLVTVYN TLSPMEPHAL VQLCGTYPPS 300  
 mEpithin ----- --V-P--- H-----D S-----V -R---FS--

hTADG15 YNLTFHSSQN VLLITLITNT ERRHPGFEAT FFQLPRMSSC GGRLRKAQGT 350  
 mEpithin -----L--- -F-V----- G---L----- K----- V-SDT---

hTADG15 FNSPYYPGHY PPNIDCTWNI EVPNNQHVKV SFKFFYLLEP GVPAGTCPKD 400  
 mEpithin -S----- --N---- K---RN--- R--L---VD- N--V-S-T--

hTADG15 YVEINGEKYC GERSQFVVTNS NSNKITVRFH SDQSYTDTGF LAEYLSYDSS 450  
 mEpithin -----GS -----S- --S---H-- --H----- -----

hTADG15 DPCPGQFTCR TGRCIRKELR CDGWADCTDH SDELNCSCDA GHQFTCKNKF 500  
 mEpithin -----M-M-K -----P-Y ---RY-R-N- T-----Q-

hTADG15 CKPLEFWVCDS VNDCGDNSDE QGCSCPAQTF RCSNGKCLSK SQQCNGKDDC 550  
 mEpithin -----G--- E-----GS- K-----PQ --K-----N-

hTADG15 GDGSDEASCP KVNVVTCTKH TYRCLNGLCL SKGNPECDGK EDCSDGSDER 600  
 mEpithin -----D S---S---Y -----Q----- T-----

hTADG15 DCDCGLRSFT RQARVVGGETD ADEGEWPWQV SLHALGQGHI CGASLISPWN 650  
 mEpithin N----- K-----N -----L -----D-

hTADG15 LVSAAHCYID DRGFRYSDPT QWTAFLGLHD QSQRSAAPGVQ ERRLKRIISH 700  
 mEpithin -----FQ- -KN-K---Y- M-----L- --K---S--- -LK-----T-

hTADG15 PFFNDFTFDY DIALLELEKP AEYSSMVRPI CLPDASHVFP AGKAIWVTGH 750  
 mEpithin -S-----S V---TV-----T-----

hTADG15 GHTQYGGTGA LILQKGEIRV INQTTCENL PQQITPRMMC VGFLSGGVDS 800  
 mEpithin ---KE----- D-M -----

hTADG15 CQGDGGPLS SVEADGRIFQ AGVVSWDGDC AQRNKGPGVYT RLPLFRDWIK 850  
 mEpithin -----A-K---M--- E----- CSSGLDQ

hTADG15 ENTGV\* (SEQ ID No. 2)  
 mEpithin RAHWGIAAWT DSRPQTPTGM PDMHTWIQER NTDDIYAVAS PPQHNPDCEL 900

hTADG15 HP (SEQ ID No. 10) 902

LOCUS HSU20428 2900 bp mRNA PRI 17-MER-1995  
 DEFINITION Human SNC19 mRNA sequence.  
 ACCESSION U20428  
 NID 91890631  
 KEYWORDS .  
 SOURCE human.  
 ORGANISM Homo sapiens  
     Eukaryota; mitochondrial eukaryotes; Metazoa; Chordata;  
     Vertebrata; Eutheria; Primates; Catarrhini; Hominoidea; Homo.  
 REFERENCE 1 (bases 1 to 2900)  
 AUTHORS Zheng,S., Cai.X., Geng,L., Cao.J., Inang,L. and Zhi,J.Z.  
 TITLE SNC19 gene in Homo sapiens  
 JOURNAL Unpublished  
 REFERENCE 2 (bases 1 to 2900)  
 AUTHORS Zheng,S.  
 TITLE Direct Submission  
 JOURNAL Submitted (30-JAN-1995) Shu Zheng, Cancer Institute, Zhejiang  
     Medical University, Hangzhou, 310033, Peoples Republic of China



TADG15: TC~~A~~GAGGCCCTGGGTACCA~~T~~GGGA~~T~~ATCGG~~C~~CC~~T~~GC~~A~~AGGG~~B~~CCCC~~G~~AG~~B~~ACTTCGGC~~G~~CGGGACT 81

SNC19: .....

92 CAAGTACAACTCCCCGGCACGAGAAGTGTATGGCTTGAGGAAGGGGT  
93 GAGTTCCCGTCAAGTCAGTCAAGAGGTGGAGAACATGGCCCCGGGG 191

82 : CAGGCTTGTCTTCATGGCTACATGAGGAACAAATTGAGAATTTCGCGGAGGCTTACGCGACTCTCCAGGCTGCTTTATAAGCTTGCCAGGCAAGGT 181

101 AGAAGGTCTTCATGGCTACATGAGGATCACAAATGAGAATTGGTGTCTTACCAACTCCAACTCACTGATTTGTAGCCTGGCCAGCPAGGT 200

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593 گلستانِ ادب، جلد ۲۰، سال ۱۴۰۰، شماره ۳۷، پیاپی ۸۸۰

9:5 CHARACTERISTICS OF THE CLOSTRIDIUM BACILLIFORMIS GROUP 107

784 C-C-A-C-T-G-A..C-C-G-G-C-A-T-C-C-G-G-C-T-T-G-A-G-G-C-A-L-C-T-T-C-L-C-T-C-L-C-T-A-G-C-T-C-A-T- 881

1374

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~~FIGURE~~ 12